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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/530,866

04/11/2005

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EXAMINER

LUKTON, DAVID

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

07/22/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/530,866	<b>Applicant(s)</b> JANSSON, JOHN-OLOV	
	<b>Examiner</b> DAVID LUKTON	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-10, 14, 15, 18, 20, 22, 27, 28, 30 and 38-41 is/are pending in the application.
- 4a) Of the above claim(s) 10, 18 and 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9, 14, 15, 22, 27, 28, 30 and 38-41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/23/08 has been entered.

Pursuant to the response filed 1/29/08, claims 1 and 38 have been amended, and claim 41 added. In view of the RCE filing, claims 39-41 are now rejoined with the elected claims.

Claims 1-10, 14, 15, 18, 20, 22, 27, 28, 30, 38-41 are now pending.

Claims 10, 18, 20, remain withdrawn from consideration; claims 1-9, 14, 15, 22, 27, 28, 30, 38-41 are examined in this Office action.



- Claim 38 is objected to because of a typographical error. The claim recites the following:

“prophylactically on therapeutically”.

Here, “on” should be “or”.

- Claim 41 is objected to because of a typographical error. The claim recites the following:

“...administering a prophylactically effective amount of ghrelin... **of** a salt thereof...”

Here, “of” should be “or”.



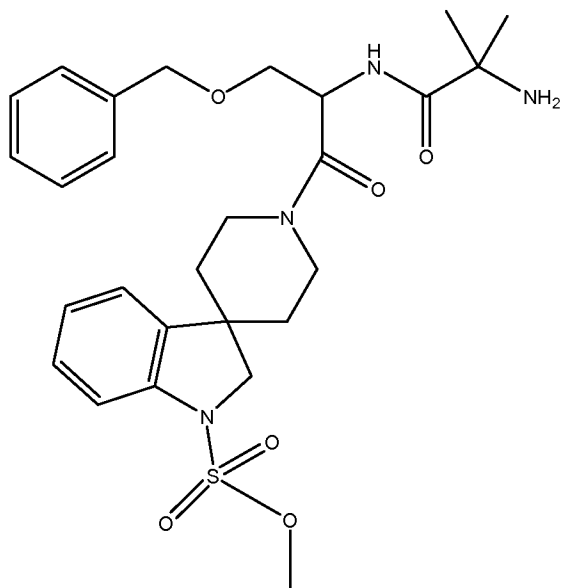
The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 14, 15, 22, 27, 28, 30, 38-41 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As indicated previously, Asakawa, A., et al., (*Gastroenterology* **120**, 337-345, 2001) discloses that once a vagotomy is performed, ghrelin loses all activity. Thus, to the extent that the claims encompass the requirement for vagotomy, enablement is lacking.

In response, applicants have argued that the pharmacological behavior of the following compound is much more indicative of what one should expect from ghrelin than ghrelin itself:



In the response filed 4/23/08, applicants have argued that somewhere in Arnold (*J. Neurosci* **26**, 11052-60, 2006) there is an experiment which supports this conclusion. However, applicants have declined to identify the passage in question.

A matter separate from the foregoing concerns claim 38. This claim recites the term “prophylactically effective”. Even if it is true that ghrelin can mitigate loss of body weight, or that ghrelin can mitigate the state of cachexia, it does not follow therefrom that outright prevention can be achieved. In response to this ground of rejection, applicants have argued that claim 38 does not recite the term “prophylactically”. However, this term is present in line 7 of claim 38. The term at issue is also present in claim 41.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary,

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amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

As matters currently stand, “undue experimentation” would be required to practice the claimed invention.



The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 14, 15, 22, 27, 28, 30, 38, 41 are rejected under 35 U.S.C. §103 as being unpatentable over (a) Zittel T. (*American Journal of Surgery* 169(2), 265-70, 1995) or (b) Saidi F (*Journal of the American College of Surgeons* 189(3), 259-68, 1999) or (c) Liedman B. (*The British Journal of Surgery* 85(4), 542-7, 1998) in view of (i) Wren

A. M. (*The Journal of Clinical Endocrinology and Metabolism* **86**(12), pp. 5992-95, 2001) or (ii) Asakawa, A., et al., (*Gastroenterology* **120**, 337-345, 2001).

As indicated previously, each of the primary references (Zittel, Saidi, Liedman) discloses that gastrectomy causes weight loss. Each of the secondary references (Wren and Asakawa) discloses that ghrelin stimulates appetite. Accordingly, it would have been obvious to administer ghrelin to reverse the adverse effects of weight loss caused by the gastrectomy.

In response to the foregoing, applicants have argued that in cases where a gastrectomy has been conducted in a subject without an accompanying vagotomy, one should assume that the digestive system of the subject more closely resembles a subject in which a vagotomy has been conducted than one in which the vagotomy has not been conducted. However, applicants have provided no reason for this conclusion.

Applicants have also argued that Asakawa “teaches away” from the claimed invention. To the extent that applicants are correct about this, Asakawa “teaches toward” a finding of lack of enablement. Furthermore, this ground of rejection is not necessarily dependent on Asakawa. There are six separate grounds of rejection here. They are the following:

Zittel in view of Wren

Saidi in view of Wren

Liedman in view of Wren

Zittel in view of Asakawa

Saidi in view of Asakawa

Liedman in view of Asakawa

Thus, three of the grounds of rejection are dependent on Asakawa, and three are not.

Applicants have also argued that their data with the amide bond-containing compound MK-0667 qualifies as “unexpected results”. While this may be true to some extent, the issue is one of competing extrapolations. On the one side, there is evidence of obviousness for ghrelin itself; on the other side is evidence about a compound which barely qualifies as a peptide at all and which compound is not even referenced in the claims. For compounds that are actually peptides, and in particular ghrelin itself, the claimed invention remains obvious.

Neither of claims 39 or 40 is rejected at the present time. If it is really true, as applicants have contented, that vagotomy is an inevitable consequence of gastrectomy, then these two claims will provide all that applicants have implied that they are seeking.



Claims 1-9, 38, 41 are rejected under 35 U.S.C. §103 as being unpatentable over (a) Zittel T. (*American Journal of Surgery* 169(2), 265-70, 1995) or (b) Saidi F (*Journal of the American College of Surgeons* 189(3), 259-68, 1999) or (c) Liedman B. (*The British Journal of Surgery* 85(4), 542-7, 1998) in view of (i) Wren A. M. (*The Journal of Clinical Endocrinology and Metabolism* 86(12), pp. 5992-95, 2001) or (ii) Asakawa,



A., et al., (*Gastroenterology* **120**, 337-345, 2001) further in view of Kojima, M. (*Nature* 402 (6762), 656-660, 1999).

As indicated above, each of the primary references (Zittel, Saidi, Liedman) discloses that gastrectomy causes weight loss. Each of the secondary references (Wren and Asakawa) discloses that ghrelin stimulates appetite. Kojima provides the sequence of ghrelin.

The rejection is maintained.



Claims 1-9, 38, 41 are rejected under 35 U.S.C. § 103 as being unpatentable over (a) Zittel T. (*American Journal of Surgery* 169(2), 265-70, 1995) or (b) Saidi F (*Journal of the American College of Surgeons* 189(3), 259-68, 1999) or (c) Liedman B. (*The British Journal of Surgery* 85(4), 542-7, 1998) in view of (i) Wren A. M. (*The Journal of Clinical Endocrinology and Metabolism* **86**(12), pp. 5992-95, 2001) or (ii) Asakawa, A., et al., (*Gastroenterology* **120**, 337-345, 2001) further in view of Hosoda, H. (*J. Biol. Chem.* **278**(1), 64-70, 2003)

As indicated above, each of the primary references (Zittel, Saidi, Liedman) discloses that gastrectomy causes weight loss. Each of the secondary references (Wren and Asakawa) discloses that ghrelin stimulates appetite.

Thus, the claims remain obvious.



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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

/David Lukton/

Primary Examiner, Art Unit 1654